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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/095,536	06/10/1998	JOHN A. KINK	OPHD-03282	9749

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/095,536	KINK, JOHN A.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.*
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-12,15-18 and 34-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-12, 15-18, 34-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 7-12, 15-18, 34-48 are pending and under consideration.

Response to Arguments

Applicant's arguments filed 03/31/2004 have been fully considered but they are not persuasive, for the reasons set forth below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7-12, 15-18, 34-48 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. patent No. 5,723,120 (Brakenhoff et al.) in view of Doherty et al. (1992) and further in view of U.S. Patent No. 5,420,253 (Emery et al.), for reasons of record set forth in the Office Action of 9/29/2003.

The claims are drawn to a method of treatment of a mammal with sepsis by administration of a combination of anti-IL-6 and anti-TNF antibodies, and also wherein the combination also includes anti-IFN antibodies, and further wherein the antibodies are derived from avian sources. The rejection of record set forth that it would have been obvious to one of skill in the art at the time the invention was made to practice a method of treating patients with sepsis with therapeutic compositions comprising anti-TNF, anti-IL-6 and anti-IFN-gamma antibodies that are avian in source.

Applicant argues that the Examiner has attempted to support the rejection with the assertion that it is merely a "design choice . . . to use either an IL-6 receptor antagonist, or antibodies to IL-6." Applicant further asserts that this is not proper examination, and that proper examination requires an evidentiary basis for selecting from the vast number of possibilities. However, the evidentiary bases for the design choice of using antibodies to IL-6 can be found within the '120 patent itself. The '120 patent discloses a method of treatment of sepsis using an IL-6 receptor antagonist (column 3, lines 17-21), which would neutralize IL-6 activity. The '120 patent further discloses that there are several ways to neutralize the activity of IL-6. One of these is by inhibiting the ligand-receptor interaction using IL-6 receptor antagonists (see column 2, lines 40-43), which is also disclosed as being useful for the treatment of sepsis. Another way to neutralize IL-6 activity, is to use antibodies to IL-6 (see column 2, lines 29-30). So, the disclosure of the effectiveness of treating sepsis with agents that inhibit IL-6 activity, and the enumeration of agents which can neutralize IL-6 activity as including both IL-6 receptor anatagonists and anti-IL-6 antibodies serves as the evidentiary basis for the design choiceof using anti-IL-6 antibodies to treat sepsis, and all this is found in the '120 patent. Applicant

further argues that there is no basis for the Examiner's statement that the '120 patent teaches "compositions comprising anti-IL-6 and anti-TNF-a antibodies". However, the '120 patent discloses that other agents may be combined with IL-6 receptor antagonists for the treatment of sepsis, including anti-TNF antibodies (see column 12, lines 44-50). Given the design choice of substituting anti-IL-6 antibodies for IL-6 receptor antagonists, this provides the basis for the combination of anti-IL-6 antibodies and anti-TNF antibodies to treat sepsis.

Applicant further submits that the references cannot be considered collectively until the Examiner points to some evidence to support combining those references, and that In re Rouffet requires the Examiner to present soundly reasoned arguments based upon the substance of the cited references. Applicant further alleges that what the Examiner has provided are unsupported and conclusory statements in a failed attempt to identify the administration of an IL-6 antibody and a TNF antibody composition for the treatment of sepsis. However, in the rejection of record, the teaching of the Doherty reference was cited as being that both TNF-alpha and IFN-gamma are important mediators of septic shock (page 1666, column 2), and that that mice treated with either anti-IFN-gamma polyclonal antibodies or anti-TNF polyclonal antibodies had a dose dependent improvement in survival after a lethal dose of LPS (page 1669, columns 1 and 2 and Figure 3 page 1667), which is an animal model of sepsis. Thus, the evidence to combine the references is provided in the Doherty reference which teaches the role of TNF and IFN in sepsis, and that sepsis can be successfully treated by administration of antibodies to either TNF or IFN, coupled with the disclosure in the '120 patent that combinations of agents including antibodies are useful in treating sepsis. Applicant further argues that Doherty et al., does not contemplate any combination of IFN-y antibodies and TNF-a antibodies in the treatment of LPS-induced

sepsis. However, the '120 patent discloses the combination of anti-TNF and anti-IL-6 antibodies, while the Doherty reference teaches the efficacy of IFN-y in treating sepsis.

Applicant further argues that Emery et al. also is of no consequence to the pending independent claims because the reference lacks any teaching for the administration of antibodies to TNF-G, IL-6 or gamma IFN, either singly or in any combination, to mammals for the treatment of sepsis. However, the '253 patent was cited as disclosing a method for purifying high yields of IgG (IgY) immunoglobulin from chicken egg yolk (see Abstract). The '253 patent discloses that antibodies derived from egg yolk provide significant advantage over their mammalian counterparts because they provide a higher level of specificity and reduced amount of undesirable side effects, and the motivation to combine this reference with the others is the disclosure that anti-TNF antibodies could be produced by this method (column 4, lines 43-44) and that these antibodies could be administered orally, parenterally or by injection when used to immunize animals or humans (column 8, lines 49-68).

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
June 23, 2004